REMARKS

Claims 78-81, 93-102, 106, and 117-181 are pending in the present application. Claims 96, 98, and 100 have been amended herein. Claims 99, 145, 157, 159-164, and 169 have been canceled herein. Upon entry of the present Amendment, claims 78-81, 93-98, 100-102, 106, 117-144, 146-156, 158, 165-168, and 170-181 will be pending.

I. The Claimed Embodiments Are Novel

A. The Ohtsuka I Reference

Claims 96, 98, 99, 100, 142, 144-146, 154, 156-158, 160, 162-164, 166, and 168-170 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 5,013,830 (hereinafter, the "Ohtsuka I reference"). The Office Action asserts that because the RNA cleavage target WS-S(+) RNA comprises 90 nucleoside subunits, it also comprises 8-50 nucleoside subunits (Office Action at page 6). Claims 99, 160, and 162-164 have been canceled herein. Applicant traverses the rejection and respectfully requests reconsideration thereof as it relates to the remaining claims because the Ohtsuka I reference does not teach every feature recited in the rejected claims.

Independent claims 96, 98, and 100 (remaining claims 142, 144-146, 154, 156-158, 166, and 168-170 are dependent thereon) have been amended to recite that each of the oligonucleotides "comprises from twelve to thirty nucleoside subunits." In contrast, the Ohtsuka I reference reports in Table 5 numerous RNA/DNA "mixed oligomers" that were used to digest a high molecular weight RNA WS-S(+) substrate. Column 9, line 38 through column 11, line 28 of the Ohtsuka I reference describes the experiments that Tables 4 and 5 summarize. The RNA/DNA "mixed oligomers" were used to digest the 90-mer WS-S(+) RNA substrate, which is shown in Table 4. In the experiment actually carried out, the WS-S(+) RNA substrate was actually a mixture of a 90-mer and a 91-mer (see, column 9, lines 55-56). The cleavage sites of each of the RNA/DNA "mixed oligomers" is shown in Table 5. Thus, only one of the oligonucleotides in the duplex formed by the RNA/DNA "mixed oligomers" and the 90-mer WS-S(+) RNA substrate "comprises from twelve to thirty nucleoside subunits."

The Office Action's interpretation of "comprises from eight to fifty nucleoside subunits" (presumably the same reasoning would be applied to "twelve to thirty nucleoside subunits") recited in the rejected claims to include an oligonucleotide that has 90 nucleoside subunits is strained at best and would vitiate any meaning of the upper limit of the range of nucleoside subunits recited in the rejected claims. Indeed, the upper limit of the number of nucleoside subunits in each of the oligonucleotides recited in the claims is now thirty. The claims do not recite a lower limit of at least eight to fifty (or twelve to thirty), as appears to be the interpretation in the Office Action. Further, the question is not "does 90 comprise 8-50," as set forth in the Office Action, but rather, "does "8-50 (or 12-30) comprise 90"? The answer is undoubtedly no. Therefore, the 90-mer WS-S(+) RNA substrate reported in the Ohtsuka I reference is not an oligonucleotide that "comprises from twelve to thirty nucleoside subunits." Thus, the Ohtsuka I reference fails to anticipate claims 96, 98, 99, and 100, or any claim dependent thereon. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be withdrawn.

B. The Froehler Reference

Claims 78, 94, 95, 99 and 101 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 5,256,775 (hereinafter, the "Froehler reference"). The Office asserts that the because Froehler reference reports RNA oligonucleotides that are 3-50 nucleotides in length and contain modifications on the 3' and 5' ends to protect from nucleases (referring to column 5, for example) which can be used to hybridize and inhibit an RNA target such as mRNA (referring to column 1 and 12, for example), the instantly claimed invention has been disclosed. Claim 99 has been canceled herein. Applicant traverses the rejection and respectfully requests reconsideration thereof as it relates to the remaining claims because the Froehler reference does not teach every feature recited in the rejected claims.

Claims 78, 94, 95, and 101 each recite that each of the oligonucleotides have a "portion having at least four consecutive ribofuranosyl residues" and that each of the oligonucleotides "comprises from eight to fifty nucleoside subunits." In contrast, the Froehler reference reports RNA oligonucleotides that are 3-50 nucleotides in length and contain modifications on the 3' and

5' ends to protect the oligonucleotide from nucleases. The only duplexes of oligonucleotides specifically disclosed in the Froehler reference are those formed between the RNA oligonucleotides that are 3-50 nucleotides in length that contain modifications on the 3' and 5' ends and complementary DNA strands which were used to study hybridization stability (see, Examples 10 and 11). These partner strands are DNA and do not have a "portion having at least four consecutive ribofuranosyl residues."

In addition, although columns 1 and 12 of the Froehler reference report intended uses of the oligonucleotides reported therein to "block protein synthesis by hydrogen bonding to messenger RNA" and to "block protein synthesis, transcription, replication of RNA and/or DNA which is uniquely associated with the disease or disorder," respectively, these portions of the Froehler reference disclose no specific duplexes, let alone duplexes in which each oligonucleotide "comprises from eight to fifty nucleoside subunits." Thus, the Froehler reference fails to anticipate claims 78, 94, 95, and 101. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be withdrawn.

C. The Ohtsuka II Reference

Claims 96, 98, 99, 100, 143, 155, 161, and 167 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Ohtsuka et al., J. Biochem., 1984, 139, 447-450 (hereinafter, the "Ohtsuka II reference"). The Office Action asserts that the Ohtsuka II reference reports double-stranded 8-mers that comprise 2'-fluoro modifications and thus anticipates Applicant's claimed invention. Claims 99 and 161 have been canceled herein. Applicant traverses the rejection and respectfully requests reconsideration thereof as it relates to the remaining claims because the Ohtsuka II reference does not teach every feature recited in the rejected claims.

Independent claims 96, 98, and 100 each have been amended to recite that each of the oligonucleotides "comprises from twelve to thirty nucleoside subunits." In contrast, the oligonucleotides reported in the Ohtsuka II reference are 8-mers. Therefore, the Ohtsuka II reference does not teach every feature recited in the rejected claims.

Thus, in view of the foregoing, the Ohtsuka II reference fails to anticipate claims 96, 98, and 100, or any claim dependent thereon. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. §102(b) be withdrawn.

II. The Specification Provides Ample Written Description Support for the Claims

Claims 78-81, 93-102, 106, and 117-181 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Applicant traverses the rejection and respectfully requests reconsideration since the specification provides ample written description of the claimed invention.

The requirements of §112, first paragraph, are met so long as: (1) the invention is described in the specification as broadly as it is claimed; and (2) the information provided in the specification is sufficient for persons of ordinary skill in the art having the specification before them to make and use the invention. *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). Indeed, the "function of the description required [under 35 U.S.C. §112, first paragraph,] is to ensure that the inventor had possession as of the filing date of the application relied on, of the specific subject matter claimed by him." *In re Edwards*, 196 U.S.P.Q. 465, 467 (C.C.P.A. 1978).

The Office Action asserts that the "claimed invention is based on the substrate for a dsRNAse from T24 cells" and that the "structure of the dsRNAse has not been disclosed" (Office Action at page 2). Each of Applicant's claims, however, recites a composition comprising a duplex of a first oligonucleotide and a second oligonucleotide. Nowhere does Applicant's claims recite the term "substrate." Applicant's claimed invention is described in the specification as broadly as it is claimed.

For example, Applicant teaches at page 30, lines 10-34 of the specification that the phrase "target RNA" shall mean any RNA that can hybridize with a complementary nucleic acid-like compound (a first oligonucleotide, for example). Applicant further teaches that the term "complementary" refers to precise pairing or sequence complementarity **between a first and a second nucleic acid-like oligomers containing nucleoside subunits**. Thus, the RNA target that hybridizes with a complementary nucleic acid-like compound can be a second nucleic acid-like oligomer. Applicant further teaches that the term "complementary" is used to indicate a

sufficient degree of complementarity such that stable and specific binding occurs between a compound of the invention (a first oligomer or oligonucleotide, for example) and a target RNA molecule (a second oligomer or oligonucleotide, for example). Thus, the modified oligonucleotides (such as the gapmers, for example) described in the specification are not limited to forming duplexes with mRNA targets. Rather, Applicant's specification teaches forming a duplex between these oligonucleotides and other oligomeric compounds. Thus, the specification clearly describes duplexes formed from a first oligonucleotide and a second oligonucleotide.

The Office Action also asserts, referring to claims 78, 80, 81, 93-96, 98-102, 117-122, 129-146, and 153-175, that the specification fails to provide sufficient written description whereby both strands of the duplex comprise eight to fifty nucleoside subunits. As recognized in the Office Action, page 7, lines 13-16 of the specification teach that the single-stranded RNA-like oligomer that is used to hybridize to the target RNA can comprise eight to fifty or twelve to thirty nucleoside subunits. Further, as stated above, the target RNA can be a second nucleic acid-like oligomer containing nucleoside subunits. Indeed, the term "complementary" contemplates **precise** pairing **between a first and a second nucleic acid-like oligomers containing nucleoside subunits**. If the pairing is precise, then the length of the first nucleic acid-like oligomer (the single-stranded RNA-like oligomer that is used to hybridize to the target RNA -- eight to fifty) can be the same length as the second nucleic acid-like oligomer (the target RNA -- eight to fifty). Further, the specification provides specific examples of duplexes in which both the first and second oligonucleotides comprise from eight to fifty or twelve to thirty nucleoside subunits (see, Example 27 and Table 1 which teach multiple 17-mer duplexes). Thus, the specification clearly describes duplexes in which both oligonucleotides comprise from eight to fifty or twelve to thirty nucleoside subunits.

In view of the foregoing, Applicant respectfully requests that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

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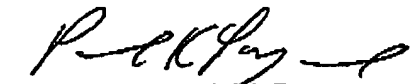
III. Conclusion

Applicant believes the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicant invites the Examiner to contact the undersigned at (215) 665-6914 to clarify any unresolved issues raised by this response.

Respectfully submitted,



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